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Claims

1. A glycosylated or nonglycosylated protein having agonist and/or antagonist activity of the formula

β^1 -(linker¹)_m- α -(linker²)_n- β^2 (1); or

β^1 -(linker¹)_m- β^2 -(linker²)_n- α (2); or

α -(linker¹)_m- β^1 -(linker²)_n- β^2 (3)

wherein each of β^1 and β^2 has the amino acid sequence of the β subunit of a vertebrate glycoprotein hormone or a variant thereof;

" α " designates the α subunit of a vertebrate glycoprotein hormone or a variant thereof;

"linker" refers to a covalently linked moiety that spaces the β^1 and β^2 subunits at distances from the α subunit and from each other effective to retain said activity, and each of m and n is independently 0 or 1.

2. The protein of claim 1 wherein said m and n are 1.

3. The protein of claim 1 wherein at least one said linker moiety includes a drug to be targeted to the receptor for the glycoprotein hormone, or wherein at least one linker is CTP or a variant thereof.

4. The protein of claim 1 wherein β^1 is the β subunit of FSH, LH or TSH extended at a position proximal to its C-terminus by a complete or partial CTP unit or variant thereof.

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5 ~~5.~~ The protein of claim 1 wherein the α subunit or one or more β subunits or both are modified by the insertion of a CTP unit or variant thereof into a noncritical region thereof and/or wherein said linker moiety includes a CTP unit or variant thereof.

5 ~~6.~~ 7. The protein of claim 1 wherein said variants contain 1-5 conservative amino acid substitutions as referred to the native forms or are truncated forms of said sequences or both.

10 ~~7.~~ 8. A pharmaceutical composition which comprises the protein of claim 1 in admixture with a suitable pharmaceutical excipient.

15 ~~7.~~ 9. The protein of claim 1 coupled to a solid support.

15 ~~9.~~ 10. Antibodies immunospecific for the protein of claim 1.

15 ~~10.~~ 11. A DNA or RNA molecule which comprises a nucleotide sequence encoding the protein of claim 1.

20 ~~11.~~ 12. An expression system for production of an agonist and/or antagonist of a glycoprotein hormone which expression system comprises a first nucleotide sequence encoding the protein of claim 1 operably linked to control sequences capable of effecting the expression of said first nucleotide sequence.

25 ~~12.~~ 13. The expression system of claim 12 which further contains a second nucleotide sequence encoding a signal peptide operably linked to the protein encoded by said first nucleotide sequence.

~~13.~~ 14. A host cell modified to contain the expression system of claim 12.

Rule
1.126

11. ~~11. 11. 11.~~

claim 13

~~14~~
~~15~~ 16.

13. A host cell modified to contain the expression system of claim 13

14. A method to produce a single-chain protein which is an agonist and/or antagonist of a glycoprotein hormone which method comprises culturing the cells of claim 14 under conditions wherein said protein is produced; and recovering said protein from the culture.

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17.

17. A method to produce a single-chain protein which is an agonist and/or antagonist of a glycoprotein hormone which method comprises culturing the cells of claim 15 under conditions wherein said protein is produced; and recovering said protein from the culture.

SECRET

add
a2